AMENDMENTS TO THE CLAIMS

This listing of claims replaces all prior versions, and listings, of claims in the application:

Listing of Claims:

1-200. (Cancelled)

201. (Currently Amended) A functional synthetic siRNA of 18-30 base pairs for interacting with a target mRNA of a target gene and silencing the target gene, the siRNA comprising:

a substantially non-functional sense strand comprising:

~~a sense region;~~

a first nucleotide of the sense strand closest to the 5' end of the sense strand having a 2'-O-alkyl modification; and

a second nucleotide of the sense strand next closest to the 5' end of the sense strand having a 2'-O-alkyl modification, wherein the rest of the sense nucleotides other then the first and second nucleotides each include a 2'-OH; and

a~~n~~ functional antisense strand ~~comprising an antisense region~~ which is at least substantially complementary with the mRNA of the target gene and the sense strand ~~region~~.

202. (Previously Presented) The siRNA of claim 201, wherein a first nucleotide of the antisense strand closest to the 5' end of the antisense strand is phosphorylated at its 5' end and the sense strand is devoid of a phosphate at its 5' end.

203. (Previously Presented) The siRNA of claim 202, further comprising a second nucleotide of the antisense strand next closest to the 5' end of the antisense strand having a 2'-OH and the first nucleotide of the antisense strand having a 2'-OH.

204. (Cancelled)

205. (Currently Amended) The siRNA of claim 202, wherein all nucleotides in the sense and antisense strands ~~regions~~ other than first and second nucleotides of the sense and antisense strands have a 2'-OH.

206. (Currently Amended) The siRNA of claim 202, wherein the antisense strand ~~region~~ includes at least one nucleotide having a 2' modification other than first and second antisense nucleotides ~~having a 2' modification~~, wherein the 2' modification in the antisense strand ~~region~~ is selected from the group consisting of 2'-O-alkyl, 2'-deoxy, 2'-amine, 2'-alkyl, and 2'-fluoro.

207. (Currently Amended) The siRNA of claim 206, wherein the 2'-O-alkyl modification on the first and second nucleotides of the sense strand is a 2'-O-methyl modification and the 2' modification on the at least one nucleotide in the antisense strand ~~region~~ is a 2'-O-methyl modification.

208. (Currently Amended) The siRNA of claim 202, wherein all nucleotides in the sense and antisense strands ~~regions~~ other than the first and second nucleotides of the sense strand each have a 2'-OH.

209. (Previously Presented) The siRNA of claim 202, wherein a third nucleotide in the sense strand has a 2'-O-alkyl modification, the third nucleotide being immediately next to the second nucleotide from the 5' end of the sense strand.

210. (Cancelled)

211. (Currently Amended) The siRNA of claim 209, wherein the 2'-O-alkyl modification is a 2'-O-methyl modification for the first, second, and third nucleotides of the sense strand and all nucleotides in the sense and antisense strands ~~regions~~ other than the first, second, and the third nucleotides of the sense and antisense strands have a 2'-OH.

212. (Cancelled)

213. (Previously Presented) The siRNA of claim 202, wherein the antisense strand has at least one phosphorothioate internucleotide linkage.

214. (Previously Presented) The siRNA of claim 202, wherein the antisense strand has at least one methylphosphonate internucleotide linkage.

215. - 219. (Cancelled)

220. (Previously Presented) The siRNA of claim 202, further comprising a 3' overhang of 1-5 nucleotides on at least one of the sense or antisense strand.

221. (Previously Presented) The siRNA of claim 220, wherein the 3' overhang has at least one phosphorothioate internucleotide linkage or at least one methylphosphonate internucleotide linkage.

222. - 223. (Cancelled)

224. (Previously Presented) The siRNA of claim 202, further comprising at least one conjugate molecule coupled to the sense or antisense strand.

225. (Previously Presented) The siRNA of claim 224, wherein the conjugate is cholesterol.

226. (Previously Presented) The siRNA of claim 225, wherein the conjugate molecule is coupled to the 3' end of the sense or antisense strand.

227. (Previously Presented) The siRNA of claim 226, wherein the conjugate is coupled to the sense strand.

228. (Currently Amended) A functional synthetic siRNA of 18-30 base pairs for interacting with a target mRNA of a target gene and silencing the target gene, the siRNA comprising:

a substantially non-functional sense strand comprising:

~~a sense region;~~

a first nucleotide of the sense strand ~~region~~ closest to the 5' end of the sense strand ~~region~~ having a 2'-O-alkyl modification and being devoid of a phosphate at its 5' end; and

a second nucleotide of the sense strand ~~region~~ next closest to the 5' end of the sense strand ~~region~~ having a 2'-O-alkyl modification, wherein the rest of the sense nucleotides other then the first and second nucleotides each include a 2'-OH; and

a~~n~~ functional antisense strand comprising:

an antisense strand ~~region~~ which is at least substantially complementary with the mRNA of the target gene and the sense strand ~~region~~; and

a first nucleotide of the antisense strand closest to the 5' end of the antisense strand having a phosphate at its 5' end.

229. (Cancelled).

230. (Previously Presented) The siRNA of claim 228, further comprising a 3' overhang of 1-5 nucleotides on at least one of the sense or antisense strand.

231. (Previously Presented) The siRNA of claim 230, wherein the antisense strand has at least one phosphorothioate internucleotide linkage or at least one methylphosphonate internucleotide linkage.

232. (Previously Presented) The siRNA of claim 228, further comprising at least one conjugate molecule coupled to the sense or antisense strand.

233. (Previously Presented) The siRNA of claim 232, wherein the conjugate is cholesterol.

234.- 236. (Cancelled)